General

Guideline Title

Screening and management of lipids.

Bibliographic Source(s)

University of Michigan Health System. Screening and management of lipids. Ann Arbor (MI): University of Michigan Health System; 2014 May. 20 p. [20 references]

Guideline Status

This is the current release of the guideline.

The guideline updates a previous version: University of Michigan Health System. Screening and management of lipids. Ann Arbor (MI): University of Michigan Health System; 2009 Feb. 15 p. [12 references]

Recommendations

Major Recommendations

Note from the University of Michigan Health System (UMHS) and the National Guideline Clearinghouse (NGC): The following guidance was current as of May 2014. Because UMHS occasionally releases minor revisions to its guidance based on new information, users may wish to consult the original guideline document for the most current version.

Note from NGC: The following key points summarize the content of the guideline. Refer to the original guideline document for additional information.

The strength of recommendation (I-III) and levels of evidence (A-D) are defined at the end of the "Major Recommendations" field.

Screening/Baseline Lipid Profile

> Patients. All men age ≥35 and women age >45 and also men age 20 to 35 and women age 20 to 45 if at increased risk for atherosclerotic cardiovascular disease (ASCVD) *[IC]*. Can also consider checking baseline lipid profile in adults ≥20 who are free from ASCVD for assessment of traditional ASCVD risk factors (age, sex, total and high-density lipoprotein cholesterol [HDL-C], systolic blood pressure [BP], use of antihypertensive therapy, diabetes, and current smoker) *[IIC]*.
>
> Fasting/non-fasting. Screening test can be obtained fasting or non-fasting to facilitate obtaining data.

Assess ASCVD Risk Factors

- Clinical ASCVD (includes stroke; peripheral arterial disease; coronary heart disease [CHD]).

- Low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL and age ≥21, not caused by drugs or underlying medical condition (see Table 1 in the original guideline document).
- Diabetes mellitus type 1 or 2, age 40 to 75 years of age with LDL-C 70 to 189 mg/dL.
- 10-year ASCVD risk ≥7.5% for ages 40 to 75 years (see Table 2 in the original guideline document for calculation information).
- Chronic kidney disease (CKD) (If CKD, see the NGC summary of the UMHS CKD guideline Management of chronic kidney disease for managing lipids in CKD patients).
- For additional risk factors to consider, see Table 3 in the original guideline document.

If No ASCVD or None of the Above Risk Factors

> Reinforce healthy lifestyle. Education as appropriate: smoking cessation, diet-exercise-weight loss, reduce excessive alcohol *[IA]*.
>
> Follow-up. Repeat screening/risk assessment in 4 to 6 years *[IID]*. If borderline, consider repeat in 1 to 2 years.

If ASCVD or Above Risk Factors Other Than CKD

> Treatment through lifestyle changes. Education as appropriate: smoking cessation (reduces coronary event rate by ~50% within 1 to 2 years), diet-exercise-weight loss, reduce excessive alcohol *[IA]*.
>
> Initiate statin therapy. (Non-statin medications should be considered only in statin-intolerant patients.)
>
> - Discuss with patient: risk reduction benefits, adverse effects, drug interactions, patient preferences.
> - Check baseline alanine transaminase (ALT) (see Table 4 in the original guideline document for monitoring abnormal baseline ALT for monitoring if liver function tests are abnormal).
> - Dosing for LDL-C reduction: high-intensity statin (≥50%), moderate-intensity statin (30%-50%). See Tables 5-8 in the original guideline document for "intensity" levels, effects, interactions, and contraindications.
> - Four main treatment benefit groups and their dosing intensity:
>   - Clinical ASCVD: age ≤75 years = high-intensity *[IA]*; age >75 years = moderate intensity *[IID]*
>   - LDL-C ≥190 mg/dL, age ≥21 = high-intensity *[IA]*
>   - Diabetes (type 1 or 2) and age 40 to 75 years with LDL-C 70 to 189 mg/dL = moderate intensity *[IA]*; can consider high-intensity if 10-year ASCVD risk ≥7.5% *[IID]*
>   - 10-year ASCVD risk ≥7.5% and age 40 to 75 years = moderate-to-high intensity *[IA]*
>   - If other risks (see Table 3 in the original guideline document), consider statin therapy based on individual benefit and harm.
> - In 6 to 12 weeks:
>   - Check lipids to evaluate adherence. Check ALT only if baseline abnormal, known liver disease, risk factors for liver disease, or on other potentially hepatotoxic medications. Check creatine kinase (CK) only if symptomatic muscle aches/weakness. If statin-intolerance, address (see Table 9 in the original guideline document).
>   - If lipids do not decrease as expected: address adherence, reinforce lifestyle modifications, and consider referral to specialist in lipid management.
>
> Triglycerides. After initiating statin therapy, if fasting triglycerides ≥500 mg/dL, consider treating.
>
> Longer term follow-up. Check lipids annually to assess adherence.

Definitions:

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

Strength of Recommendation

I. Generally should be performed
II. May be reasonable to perform
III. Generally should not be performed

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Atherosclerotic cardiovascular disease (ASCVD) including:

- Stroke
- Peripheral arterial disease (PAD)
- Coronary heart disease (CHD)

Guideline Category

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Cardiology

Family Practice

Geriatrics

Internal Medicine

Nursing

Preventive Medicine

Intended Users

Advanced Practice Nurses

Dietitians

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To present recommendations for primary and secondary prevention of atherosclerotic cardiovascular disease (ASCVD) by outlining strategies for

lipid screening, identifying patients who would benefit from treatment, and recommending appropriate treatment regimens

Target Population

Adults 20 to 79 years of age without familial or severe dyslipidemias or chronic kidney disease (CKD)

Interventions and Practices Considered

1. Screening with fasting/non-fasting baseline lipid profile
2. Assessment of clinical atherosclerotic cardiovascular disease (ASCVD) risk factors
3. Lifestyle modifications (weight loss, exercise, smoking cessation)
4. Statin therapy (non-statin medications in statin-intolerant patients)
5. Treatment of triglycerides ≥500 mg/dL
6. Referral to specialist in lipid management (if indicated)
7. Long term follow-up/repeat screening

Major Outcomes Considered

- Total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides levels
- Incidence of coronary heart disease (CHD) and stroke, and rate of coronary events
- Total mortality associated with CHD
- Drug interactions and adverse effects

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The literature search for this update began with results of the literature searches performed in 1999 for the 2000 version of this guideline and in 2007 for the 2009 update of this guideline. Since that time the American Association of Clinical Endocrinologists performed a search of relevant literature through early 2011 in developing its guidelines for management of dyslipidemia and prevention of atherosclerosis (see references in the original guideline document). Those results were used for the literature through 12/31/10. For more recent literature, a search similar to those previously performed for this guideline was conducted on Medline prospectively using the overall keywords of: *cholesterol (including hyperlipidemia, lipoproteins, HDL cholesterol), consensus development conferences, practice guidelines, guidelines, outcomes and process assessment (health care); clinical trials, controlled clinical trials, multicenter studies, randomized controlled trials, cohort studies; adults; English language; and published from 1/1/2011 to 4/30/2013.* In addition to the overall terms, for primary prevention a major search term was primary prevention of coronary artery disease with specific topic searches for: screening, pharmacotherapy, diet, exercise, alternative or complementary medicines, and other treatment. In addition to the overall terms, for secondary prevention a major search term was secondary prevention (treatment only) of coronary artery disease, peripheral vascular disease, or cerebral vascular disease/stroke with specific topic searches for pharmacotherapy, diet, exercise, alternative or complementary treatment, and other treatment. An additional search using the overall terms was performed for statins and drug interactions and for individual differences and class effects of statins.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Conclusions were based on prospective randomized controlled trials (RCTs) if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

I. Generally should be performed
II. May be reasonable to perform
III. Generally should not be performed

Cost Analysis

- Statins are not considered cost effective in the low risk group, but may be cost effective in the intermediate risk group.
- For patients with diabetes and no other atherosclerotic cardiovascular disease (ASCVD) risk factors, statin therapy may reasonably be delayed until age 40 since statin use in this population is only marginally cost effective.
- Ezetimibe should only be considered for patients intolerant to statin, niacin, fibrates, and resins, all of which have better evidence supporting

their use and are more cost effective.
- There are arguments concerning age recommendations for lipid screening that there is no evidence that screening or treating young adults has been shown to be of benefit, and given their low absolute risk, would not be cost effective.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Family Medicine, General Medicine, and Cardiology. The final version was endorsed by the Clinical Practice Committee of the University of Michigan Faculty Group Practice and the Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

Conclusions were based on prospective randomized controlled trials (RCTs) if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate screening and management of lipids in order to prevent atherosclerotic cardiovascular disease (ASCVD) and stroke

Potential Harms

- Statins:
  - The most common adverse effect from statins is muscle aches. No evidence indicates that myalgias are more common with one statin than another. Rhabdomyolysis is a life threatening complication of statin therapy, with a 10% mortality rate. The average incidence per 10,000 person-years for monotherapy is 0.44. For patients with known risk factors for rhabdomyolysis, including those with hypothyroidism, chronic renal insufficiency, and those over age 65, who require low-density lipoprotein cholesterol (LDL-C) lowering greater than can be achieved with simvastatin 40 mg, atorvastatin or rosuvastatin may be considered as alternatives (see the original guideline document for information about adverse effects associated with high-dose simvastatin and statin interactions with other medications).
  - The American College of Cardiology/American Heart Association (ACC/AHA) guideline on the treatment of blood cholesterol notes that the main adverse consideration is the excess risk of diabetes – about 0.1 excess case per 100 individuals treated with a moderate-intensity statin for 1 year and about 0.3 excess cases per 100 individuals treated with a high-intensity statin for 1 year. Both statin-treated and placebo-treated participants experienced the same rate of muscle symptoms. The actual rate of statin-related muscle symptoms in the clinical population is unclear.
  - Characteristics predisposing individuals to statin adverse effects include multiple and serious co-morbidities including impaired renal or hepatic function, history of previous statin intolerance or muscle disorders, unexplained alanine transaminase (ALT) elevations >3X upper limit of normal (ULN), or concomitant use of drugs affecting statin metabolism, and age >75 years. If any of these predisposing

characteristics are present, moderate-intensity statin therapy is recommended in individuals whom high-intensity statin therapy would otherwise be recommended. High-intensity statin therapy should also be used cautiously in patients of Asian ancestry or with a history of hemorrhagic stroke.

- Adverse effects are common with resins, and are dose dependent. The most common side effects are bloating, nausea, constipation, and abdominal pain. Resins interfere with absorption of fat-soluble vitamins and many drugs.
- Adverse effects of niacin include flushing, pruritus, gastrointestinal (GI) disturbances, fatigue, glucose intolerance, and gout. Hepatic toxicity has been reported, particularly with sustained release products at doses >2 gm/day. Niacin should be avoided in patients with underlying liver disease or uncontrolled diabetes.
- Adverse effects of fibrates are generally GI, including nausea, dyspepsia, and change in bowel habits. The risk of cholestasis and cholecystectomy is increased. Fibrates carry a small risk of myopathy as monotherapy, but the risk is increased markedly when gemfibrozil is combined with statins. Fibrates may cause a small reversible increase in creatinine, and dose adjustment in renal insufficiency.
- For patients with known coronary heart disease (CHD), exercise must be tailored to the degree of disease. Aerobic exercises (walking, cycling, swimming) should be done at levels that do not precipitate cardiac ischemia and angina.
- Further information concerning general cautions about drug class and drug interactions are provided in Table 6 and Table 7 in the original guideline document.

Contraindications

Contraindications

- Treatment with statins, niacin, and ezetimibe are contraindicated during pregnancy and lactation
- Niacin is contraindicated in hepatic disease.
- Nicotine replacement therapy is contraindicated in unstable angina or acute myocardial infarction (MI).
- Fibrates are contraindicated in severe renal or liver disease, pregnancy, or preexisting gall bladder disease.
- Contraindications and dose limitations for simvastatin and lovastatin are presented in Table 8 in the original guideline document.

Qualifying Statements

Qualifying Statements

These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2000 May (revised 2014 May)

Guideline Developer(s)

University of Michigan Health System - Academic Institution

Source(s) of Funding

University of Michigan Health System

Guideline Committee

Lipid Therapy Guideline Team

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Financial Disclosures/Conflicts of Interest

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Guideline Status

This is the current release of the guideline.

The guideline updates a previous version: University of Michigan Health System. Screening and management of lipids. Ann Arbor (MI): University of Michigan Health System; 2009 Feb. 15 p. [12 references]

Guideline Availability

Electronic copies: Available from the University of Michigan Health System Web site .

Availability of Companion Documents

Continuing Medical Education (CME) information is available from the University of Michigan Health System Web site .

Patient Resources

The following is available:

- What you need to know about high blood cholesterol. Ann Arbor (MI): University of Michigan Health System; 2014 May 1. 5 p. Electronic copies: Available from the University of Michigan Health System (UMHS) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on January 26, 2001. The information was verified by the guideline developer on March 12, 2001. This summary was updated on September 6, 2001 following the withdrawal of the drug Baycol (Cerivastatin). This summary was updated again on January 19, 2004. The information was verified by the guideline developer on February 6, 2004. This summary was updated by ECRI Institute on July 13, 2009. The updated information was verified by the guideline developer on July 21, 2009. This summary was updated by ECRI

Institute on June 27, 2011 following the U.S. Food and Drug Administration advisory on Zocor (simvastatin). This summary was updated by ECRI Institute on April 13, 2012 following the U.S. Food and Drug Administration advisories on Statin Drugs and Statins and HIV or Hepatitis C drugs. This summary was updated by ECRI Institute on September 11, 2014.

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